

9

Docket No. G-085US04CON
Serial No. 09/818,260Remarks

Claims 1-39 were initially pending in the subject application. In response to a restriction requirement, claims 1-9 were elected for examination. By way of the amendment of this date, claims 1, 4, and 7 have been amended, claims 2, 3, 5, 6, and 8-39 have been canceled, and claims 40-50 have been added. Therefore, claims 1, 4, 7, and 40-50 are now before the Examiner for consideration. Certain of the claims have been amended for the purpose of expediting the patent application process in a manner consistent with the Patent and Trademark Office Patent Business Goals (PBG), 65 Fed. Reg. 54603 (September 8, 2000), in order to correct antecedent basis issues the claimed subject matter, advance prosecution, and facilitate the business interests of Applicant(s). Support for these new claims and the amendments to the pending claims can be found throughout the subject specification, including, for example, the claims as originally filed. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Applicants note the objection to the specification set forth in the Office Action of December 3, 2003. Applicants respectfully submit that a preliminary amendment addressing this issue was filed in the Patent Office on March 17, 2003. Attached hereto is a copy of the aforementioned preliminary amendment as well as confirmation of its receipt by the Patent Office and entry of this paper is respectfully requested. Applicants respectfully request reconsideration and withdrawal of the objection in view of these papers.

Claims 1-6 have been rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. Particularly, claims 1-3 have been rejected on the basis that the claims are directed to purely mathematical and theoretical exercises that result in the manipulation of data and that the claimed method fails to result in a useful, tangible, and concrete result. Claims 3-6 have been rejected in the basis that the "system", as claimed, can be viewed simply as data. The Office Action argues that a piece of paper with written instructions for the method, or a non-computer-executable text file with instructions for the method are both just data, but are also a system for executing the method. Applicants respectfully traverse.

Applicants respectfully submit that the issue as relates to the claims being related to purely mathematical and theoretical exercises is moot in view of the amendment of claim 1. As the Patent

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10

Docket No. G-085US04CON
Serial No. 09/818,260

Office is aware, methods that require the measurements of physical objects or activities to be transformed outside of the computer into computer data constitute patentable subject matter. In the case of the instant invention, genetic material from individuals is sequenced and biallelic markers are identified. A haplotype is then assigned to an individual and the haplotypes of individuals is then analyzed according to the methods of the subject invention. The analysis of these haplotypes can then be used to associate various haplotypes with a trait or phenotype. Thus, it is respectfully submitted that the amended claims constitute patentable subject matter as the claimed methods provide for a useful, tangible, and concrete result (namely, the association of various haplotypes with a trait or phenotype). Accordingly, reconsideration and withdrawal of the rejection as applied to claim 1 is respectfully requested.

Turning to the rejection as applied to claims 4-6, it is respectfully submitted that the claims, as originally presented, are directed to statutory subject matter. As the Patent Office is aware, an explicit definition provided by the applicant for a term will control interpretation of the term as it is used in the claim. *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301, 53 USPQ2d 1065, 1069 (Fed. Cir. 1999) and it is submitted that the meaning assigned to the claimed "system" by the Patent Office is inconsistent with the definitions provided in the specification of the subject application.

For example, the specification (at page 16, lines 17-19, page 17, lines 17-27, and page 22, lines 21 through page 23, line 14) indicates that:

Instructions refer to computer-implemented steps for processing of information in the system. Instructions can be implemented in software, firmware, or hardware and include any type of programmed step undertaken by components and modules of the system.

The system may include any type of electronically connected group of computers including, for instance, the following networks: Internet, Intranet, Local Area Networks (LAN) or Wide Area Networks (WAN). In addition, the connectivity to the network may be, for example, remote modem, Ethernet (IEEE 802.3), Token Ring (IEEE 802.5), Fiber Distributed Datalink Interface (FDDI) or Asynchronous Transfer Mode (ATM). Note that computing devices may be desktop, server, portable, hand-held, set-top, or any other desired type of configuration. As used herein, an Internet includes network variations such

11

Docket No. G-085US04CON

Serial No. 09/818,260

as public internet, a private internet, a secure internet, a private network, a public network, a value-added network, an intranet, and the like.

The system may be used in connection with various operating systems such as: UNIX, Disk Operating System (DOS), OS/2, Windows 3.X, Windows 95, Windows 98, Windows 2000 and Windows NT.

The various software aspects of the system may be written in any programming language such as C, C++, BASIC, Pascal, Perl, Java, and FORTRAN and ran under the well-known operating system. C, C++, BASIC, Pascal, Java, and FORTRAN are industry standard programming languages for which many commercial compilers can be used to create executable code.

A system preferably includes one or more computers and associated peripherals that carry out selected functions. For example, a User system preferably includes the computer hardware, software and firmware for executing the specific software instructions described below. A system should not be interpreted as being limited to be a single computer or microprocessor, and may include a network of computers, or a computer having multiple microprocessors.

Accordingly, embodiments of the present invention identify haplotypes using a binary (e.g., two state) code. A convention is set such that all possible haplotypes are coded with binary mask arrays. For example, for a given loci A/T, the haplotypes is 0 if the base is A and is 1 if the base is T. More generally, for each possible site, the first base in alphabetical order is 0 and the other base is 1. With this convention, all of the haplotypes can be coded with binary mask arrays. For example, if there are 5 SNPs: A/T C/G C/T A/G C/G, the haplotype ACTGC will be coded 00110.

There are two main advantages to this way of coding: 1) All operations on haplotypes become faster because binary operations are the most efficient ones due to the internal structure of the computer. Thus, efficient processes to generate/manipulate those haplotypes can be implemented. 2) In the algorithm and in its implementation in the program, you need to create some arrays that will store information about haplotypes. Those arrays are composed of cells. It is important to keep track of which cell contains information about which haplotype. With a binary implementation, this problem no longer exists because for computers, binary mask arrays and integers are the same (more precisely, integers are stored in memory with binary numbers). So cells in arrays can be directly accessed with the haplotype itself.

For example, the haplotype ACTGC is coded 00110, which

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12

Docket No. G-085US04CON
Serial No. 09/818,260

corresponds to 6 in decimal integer form. If information about its frequency is stored in the 6th cell of the array containing all frequencies, then there is a direct relation between the haplotype and its frequency. There is no need to keep track of which cell contains which information. This becomes implicit, thus increasing the efficiency of the program. This way of coding is particularly powerful for long haplotypes.

As the Patent Office is aware, computer-readable medium (or a system comprising at least one computer) containing a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized is statutory subject matter. In the case of the instant invention, it is respectfully submitted that the functionality of the computer (*e.g.*, allowing one skilled in the art to draw a statistical inference between at least two groups of individuals). Accordingly, reconsideration and withdrawal of the rejection is respectfully requested.

Claims 2-3, 5-6, and 8-9 have been rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully submit that this rejection is moot in view of the cancellation of the claims and the presentation of new claims. Accordingly, withdrawal and reconsideration of the rejection is respectfully requested.

Claims 1-9 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Stanton (US 2002/003990 A1) in view of Blumenfeld *et al.* (US 6528260 B1). The Office Action argues that Stanton teaches a method of determining the statistical significance of a difference between haplotype frequency profiles of at least two groups of individuals comprising determining the combined likelihood that said at least two groups of individuals are derived from the same distribution of haplotypes and determining the difference of said sum and said combined likelihood. The Office Action further argues that Stanton teaches the use of permutation tests for statistical analysis, the use of a chi square test in determining the difference between said sum and said combined likelihood and the use of an odds ratio in statistical hypothesis testing. The Office Action also indicates that Stanton fails to specifically teach: a) randomly permuting the haplotypes between the groups to determine the probability that the groups do not come from the same distribution of haplotypes; b) calculation of all possible single haplotype chi square tests; or c) assessing the statistical significance of individual haplotypes using an odds ratio or a P-excess value. The Office

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13

Docket No. G-085US04CON
Serial No. 09/818,260

Action attempts to remedy these defects with the teachings of Blumenfeld *et al.* where it is argued that the reference teaches determining the statistical significance of a haplotype analysis by simulating hypothetical groups, randomly permuting the haplotypes between groups to determine the probability that the groups do not come from the same distribution of haplotypes, calculating all possible single haplotype chi-square tests, and addressing the statistical significance of individual haplotypes using an odds ratio. The Office Action argues that it would have been obvious to one of ordinary skill in the art to incorporate the teachings of Blumenfeld *et al.* into the teachings of Stanton in order to confirm the statistical significance of first stage haplotype analysis; determine if there is a statistically significant correlation between the haplotype and phenotype under study; and to determine if there is an association between a risk factor and a disease. Applicants respectfully traverse.

As the Patent Office is aware, all the claim limitations must be taught or suggested by the prior art to establish the *prima facie* obviousness of a claimed invention. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (CCPA 1974). In the case of the subject invention it is respectfully submitted that the rejection of record fails to teach or suggest all the claim limitations of the subject invention. For example, the combination of references fails to teach coding haplotypes of individuals with a binary code, binary mask arrays or identifying the haplotypes of all individuals in each of said at least two groups with a binary code. Applicants further submit that the claimed invention is unexpectedly superior as compared to the methods taught in the prior art. For example, the computer implemented methods of the subject invention are computationally more efficient and faster than those of the prior art (see, for example, specification, page 21, line 28, through page 23, line 27). As such, it is respectfully submitted that the combination of references has not established the *prima facie* obviousness of the claimed invention and reconsideration and withdrawal of the rejection is respectfully requested.

It should be understood that the amendments presented herein have been made solely to expedite prosecution of the subject application to completion and should not be construed as an indication of Applicants' agreement with or acquiescence in the Examiner's position. Applicants expressly reserve the right to pursue the invention(s) disclosed in the subject application, including

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14

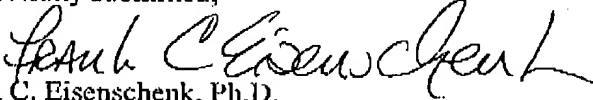
Docket No. G-085US04CON
Serial No. 09/818,260

any subject matter canceled or not pursued during prosecution of the subject application, in a related application.

In view of the foregoing remarks and the amendments to the claims, Applicants believe that the pending claims are now in condition for allowance, and such action is respectfully requested. The Commissioner is hereby authorized to charge any fees under 37 C.F.R. 1.16 or 1.17 as required by this paper to Deposit Account 19-0065.

Applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,


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Attachment: Copy of Preliminary Amendment dated March 17, 2003 and Transaction Report confirming receipt by the Patent Office